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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/746,713	12/21/2000	Yasuo Ohdaira	00629CIP/LH	1181

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EXAMINER

LEE, SHUN K

ART UNIT	PAPER NUMBER
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2884

DATE MAILED: 01/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/746,713

Applicant(s)

OHDAIRA ET AL.

Examiner

Shun Lee

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 November 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 December 2000 and 17 March 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. 09/652,500.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baer (US 5,866,911) in view of Marcu *et al.* (US 6,272,376), Deka *et al.* (US 5,909,278), and Alexander (US 6,522,345).

In regard to claims **16** and **20**, Baer discloses (Fig. 7) a laser scanning microscope comprising:

(a) a pulse laser unit (70) configured to oscillate a pulse laser beam to excite a sample (19);

(b) a scanning mirror (16) configured to scan the pulse laser beam;

- (c) a photodetector (23; which may be a photomultiplier tube; column 4, lines 31-36) configured to detect light from the sample (19) and output a photodetector detection signal;
- (d) a sampling control circuit (74, 75, 76) which receives a pulse oscillation signal (*i.e.*, detect oscillation of the pulse laser beam) from the pulse laser unit (70) and generates a trigger signal delayed by a predetermined time (*i.e.*, electrically adjusting to provide an interval from zero to several picoseconds; column 11, lines 37-44); and
- (e) a memory (24) which stores the photodetector detection signal; and
- (f) an image display unit (26) which reads the data from the memory (24) and displays the read data as an image in synchronism with each scanned position by the laser beam (column 4, lines 31-39).

While Baer also discloses (column 11, lines 8-12) that "laser dyes and their local environments can be characterized by fluorescence lifetime measurements, with minimal additional equipment costs", the microscope of Baer lacks that the additional equipment for fluorescence lifetime measurements comprise an A/D converter which converts the photodetector detection signal to digital data in synchronism with sampling pulse signals generated during a less than 10 nsec predetermined output period required for data acquisition only to obtain a fluorescent decay curve with one excitation of a fluorescent signal, wherein the sampling pulse signals are generated by a pulse generator for each trigger signal received from the sampling control circuit. However, equipment for fluorescence lifetime measurements such as conventional commercially

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available digital oscilloscopes (comprising A/D converters and pulse generators) are well known in the art. For example, Marcu *et al.* teach (column 7, lines 11-56) equipment for fluorescence lifetime measurements comprise a conventional commercially available digital oscilloscope (*i.e.*, Tektronix TDS 620A) which is triggered to capture the photodetector (*i.e.*, photomultiplier tube 20) detection signal. Further, Deka *et al.* teaches (column 7, lines 9-12; column 9, lines 51-65) to provide an adjustable excitation pulse repetition rate to accommodate different fluorescence decay times and that only one pulse from each fluorescent pulse train was required for fluorescence decay analysis. In addition, Alexander teaches (column 1, lines 15-29; column 3, lines 59-62; column 7, lines 26-28; column 8, lines 3-19) that a conventional (commercially available) digital oscilloscope sample and record time varying analog signals (*i.e.*, voltage signals as a function of time) using well-known analog-to digital conversion electronics driven by a time base (*i.e.*, pulse generator) which is triggered by a trigger signal as is well known in the art and that the selection of the portion (*i.e.*, predetermined output period) of the analog input signal which is sampled and stored is determined by appropriate triggering circuitry to enable the operator to display the desired portion of the waveform. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide additional equipment such as a conventional commercially available digital oscilloscope (comprising well known pulse generators and A/D converters) in the microscope of Baer and to adjust the excitation pulse repetition rate to one excitation pulse per 10 nsec, in order to measure a less than 10 nsec fluorescence decay.

In regard to claim **17** which is dependent on claim 16, the microscope of Baer lacks that digital integration of a fluorescent signal is performed using the digital data stored in the memory. However, analysis of time-resolved fluorescence data is well known in the art. For example, Marcu *et al.* teach (column 4, lines 42-54; column 8, lines 23-54) that fluorescent intensity data at a given wavelength can be obtained by integrating the intensity decay curve at the given wavelength. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to digitally integrate a intensity decay curve stored in the memory of Baer, in order to obtain fluorescence intensity at a desired wavelength.

In regard to claims **18** and **19** which are dependent on claim 16, the microscope of Baer lacks that analysis is performed to detect a peak or a time constant of a fluorescent signal using the digital data stored in the memory. However, analysis of time-resolved fluorescence data is well known in the art. For example, Marcu *et al.* teach (column 4, lines 42-54; column 8, lines 23-54) that data analysis comprise of determining peak amplitudes and time constants in order to make the information more manageable. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to analyze the intensity decay curves stored in the memory of Baer, in order to determine peak amplitudes and time constants so as to reduce the information to a more manageable form.

Response to Arguments

4. Applicant's arguments filed 22 November 2005 have been fully considered but they are not persuasive.

Applicant argues that Baer does not explain whether the fluorescence lifetime measurements read each and every pixel of scanning images in the laser scanning microscope. Examiner respectfully disagrees. Baer states (column 16, line 60 to column 17, line 5) that "The examples given have considered a specimen or target material with just one radiationally excitable species, however it is often useful in fluorescent microscopy of biological material to employ two or more contrasting fluorescent stains, and the present invention could be used in such applications, for example by choosing two fluorophores which have the same excitation and quenching wavelengths but differ in fluorescent lifetimes or emission spectra. All the examples given have employed scanning of a spot or line, but the present invention is also applicable to applications requiring selective illumination of just a single unscanned spot". Thus Baer expressly teaches both measurement of a single unscanned spot and a plurality of measurements (e.g., fluorescent lifetimes) during scanning for fluorescent microscopy of biological material.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any


extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shun Lee whose telephone number is (571) 272-2439. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Porta can be reached on (571) 272-2444. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL


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